8EHQ-1093-0394

Larry R. Zobel, MD, MPH
Medical Director

3M Medical Department

3M Center, Building 220-2E-02
St. Paul, MN 55144-1000
612 733 5181 Office
612 733 1773 Facsimile

8e HQ Suppt.

3M

October 11, 1993

Contains No CBI

EPA-OTS

000829750V

Express Mail - Return Receipt Requested

Document Processing Center (TS-790)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

8EHQ-0381-0394
SPD: 89941000007

Re: TSCA 8(e) SUPPLEMENTAL NOTICE:

8EHQ-0381-0394
Mixture of Ammonium Perfluorooctanoate (CAS 3825-26-1),
Ammonium Perfluoroheptanoate (CAS 6130-43-4),
Ammonium Perfluorohexanoate (CAS 21615-47-4) and
Ammonium Perfluoropentanoate (CAS 68259-11-0)
or (Ammonium Perfluoroalkyl carboxylates)

Dear Coordinator:

On September 23, 1993, 3M was informed by DuPont of preliminary results of a recently completed study that basically corroborates findings in the testis of an earlier 3M study, "Two Year Oral (Diet) Toxicity/Carcinogenicity Study of Fluorochemical FC-143 in Rats," previously submitted to the Agency [see TSCA 8(e) file 8EHQ-0381-0394]. At the comparable dose level used in both studies and in male rats, liver tumors were also increased; however, while only pancreatic atrophy was seen in the 3M study, there was a 9.2% increase in pancreatic acinar cell adenomas reported in the DuPont study. These two findings represent new information which may or may not have biological implications for extrapolation to humans. A comparison of actual incidence values for both studies is shown in Table 1.

The preliminary results are from a recently completed mechanistic two-year bioassay in rats which was conducted at DuPont Haskell Laboratory using Ammonium Perfluoro-alkyl carboxylates manufactured by 3M.

5 pgs

Ammonium Perfluoroalkyl carboxylates were included in a mechanistic bioassay investigating extra hepatic tumor induction by compounds which induce peroxisome proliferation. Ammonium Perfluoroalkyl carboxylates (93 to 97% ammonium perfluorooctanoate) were purchased as a product from 3M and are used by DuPont Polymers. In this mechanistic bioassay, 300 parts per million Ammonium Perfluoroalkyl carboxylates was fed to rats as a part of their diet for two years. In addition to an *ad libitum* control, a second control group was pair-fed to the 300 ppm Ammonium Perfluoroalkyl carboxylates group to control for the effects of reduced body weight. Increased incidences of combined (single, multiple) hepatic adenomas, Leydig cell adenomas, and pancreatic acinar cell adenomas were seen in the 300 ppm Ammonium Perfluoroalkyl carboxylates group when compared to either the *ad libitum* or pair-fed controls (Table 2). The tumor incidences (liver, testis, pancreas) were outside the historical control incidence range for DuPont Haskell Laboratory. In addition, age-adjustment statistics also support the conclusion that the tumor incidence was elevated for the liver (both controls), pancreas (pair-fed control), and testis (pair-fed control).

In the previous two-year feeding study conducted by 3M, an increased incidence of Leydig cell adenomas was reported at 300 ppm Ammonium Perfluoroalkyl carboxylates. The Leydig cell adenoma incidence in the 3M study was 0% (*ad libitum control*), 4% (30 ppm), and 14% (300 ppm Ammonium Perfluoroalkyl carboxylates). There was no reported increase in tumors of the liver or pancreas; however, the liver of the rat is recognized as a primary target organ associated with other studies of this material.

Under these experimental conditions, the effects described above would appear to be reportable based on EPA guidance regarding TSCA 8(e) criteria.

In response to this data, 3M is notifying customers known to purchase this material to review their handling practices to make certain that they are consistent with recommendations on the material safety data sheet. The subject MSDS has been revised to reflect these new findings from DuPont Haskell Laboratory.

Very truly yours,

Larry R. Zobel, M.D.
Medical Director

bh (RGP1CJ-EPADUPON)

Enclosures:

1. Table 1 - Tumor Incidence Values
2. Table 2 - Summary of Hyperplasia/Neoplasia Lesion Incidence in the Liver, Pancreas, and Testis

c: Charles F. Reinhardt, M.D.
DuPont Haskell Laboratory
(FAX: 302-366-5207)

Sharron Laas
DuPont Polymers & Automotive
(FAX: 302-999-4731)

TABLE 1

TUMOR INCIDENCE VALUES
Male Rats (%)

LESION	D u P o n t			3 M	
	Con	P-F Con*	300 ppm	Con	300 ppm
Liver n =	80	79	76	50	50
Adenoma	2.5	1.3	13.1	0	0
Carcinoma	0	2.5	0	6	10
Combined Aden./Carcin.	2.5	3.8	13.1	6	10
Testes n =	79	78	76	50	50
Leydig cell adenoma	0	2.6	10.5	0	14
Leydig cell hyperplasia	13.9	33.3	46.0	0	0
(Tubular atrophy)	-	-	-	14	22
Pancreas n =	80	79	76	50	50
Acinar cell adenoma	0	1.3	9.2	0	0
(Acinar cell atrophy)	-	-	-	13	22
Thyroid n =				50	50
C-cell adenoma				0	9
C-cell carcinoma				5	0
Combined aden./carcin.				5	9
Adrenal n =				50	
Pheochromocytoma				4	

* Pair-fed Controls
( ) Non-tumor Findings

(RGP125-CEPADUP2)

TABLE 2

SUMMARY OF HYPERPLASIA/NEOPLASIA LESION INCIDENCE IN THE LIVER, PANCREAS, AND TESTIS DU PONT STUDY

LESION	AD LIBITUM CONTROL	PAIR-FED CONTROL	300 PPM**
LIVER:			
Adenoma	2/80 (2.5)a	1/79 (1.3)	7/76 (9.2)#
Multiple Adenoma	0/80 (0)	0/79 (0)	3/76 (3.9)
Combined Adenomas	2/80 (2.5)	1/79 (1.3)	10/76 (13.1)*#
Carcinoma	0/80 (0)	2/79 (2.5)	0/76 (0)
Adenoma/Carcinoma Combined	2/80 (2.5)	3/79 (3.8)	10/76 (13.1)*#
PANCREAS:			
Acinar Cell Adenoma	0/80 (0)	1/79 (1.3)	4/76 (5.2)
Multiple Acinar Cell Adenoma	0/80 (0)	0/79 (0)	3/76 (3.9)
Combined Adenomas	0/80 (0)	1/79 (1.3)	7/76 (9.2)*#
Acinar Cell Carcinoma	0/80 (0)	0/79 (0)	1/76 (1.3)
Adenoma/Carcinoma Combined	0/80 (0)	1/79 (1.3)	8/76 (10.5)*#
Acinar Hyperplasia	14/80 (17.5)	8/79 (10.1)	30/76 (39.5)*#
TESTIS:			
Leydig Cell Adenoma	0/79 (0)	2/78 (2.6)	8/76 (10.5)*#
Leydig Cell Hyperplasia	11/79 (13.9)	26/78 (33.3)	35/76 (46.0)*

a Incidence (percent of animals in group).

* $p < 0.05$ compared to *ad libitum* control (Fisher's Exact test).

# $p < 0.05$ compared to pair-fed control (Fisher's Exact test).

** Ammonium Perfluoroalkyl carboxylates.

(RGP125-CEPADUP)